

Amendments to the Specification

I. Please add the following new paragraphs after paragraph [0032]:

[0033] Figure 15 illustrates general methods that can be used for preparation of compounds of the invention having a secondary pharmacophore that is a ketone functional group. (a) Benzophenone imine, CH_2Cl_2 , rt; (b) DIBAL, THF, -78°C ; (c) Mg/I_2 , hexylbromide, THF, rt; (d) acetic anhydride, DMSO, rt; (e) 1N HCl/dioxane, rt; (f) 3-chlorophenyl isocyanate, TEA, DMF, rt.

[0034] Figure 16 shows how a variety of compounds having a secondary pharmacophore that is either an ester or amide functional group can be prepared. (a) aryl or alkyl isocyanate, DMF, rt; (b) bromopentane, K_2CO_3 , NaI, acetonitrile, reflux; (c) di-t-butyl dicarbonate, dioxane, 50°C ; (d) pentylamine, isobutyl chloroformate, NMM, DMF, rt; (e) 4M hydrochloric acid, dioxane; (f) 3-chlorophenyl isocyanate, TEA, DMF, rt.

[0035] Figure 17 illustrates a variety of methods for introducing secondary pharmacophores that are esters, amide, ureas, carbonates and carbamates, from readily accessible starting materials. (a) 3-chlorophenyl isocyanate, DMF, rt; (b) heptanoic anhydride (761), chloroformic acid pentyl ester (760), or pentyl isocyanate (762), TEA, DMF, rt; (c) di-t-butyl dicarbonate, dioxane, rt; (d) heptanoic anhydride (765), chloroformic acid pentyl ester (777), or pentyl isocyanate (766), DMF, rt; (e) 4M HCl, dioxane; (f) 3-chlorophenyl isocyanate, TEA, DMF, rt.

[0036] Figure 18 illustrates pathways for the introduction of a tertiary pharmacophore that is an ester or an amide functional group. (a) adamantyl isocyanate, chloroform, reflux; (b) alkyl or aryl halide, K_2CO_3 , NaI, acetonitrile, reflux; (c) alcohol or amine, isobutyl chloroformate, TEA, DMF, rt; (d) t-butanol, EDCl, DMAP, methylene chloride, rt.

II. Please replace original paragraph [0122] with the following amended paragraph:

[0122] The compounds of the present invention can be prepared by a variety of methods as outlined generally in ~~the schemes below~~ Figures 15-18.

III. Please replace paragraph [0123] and its heading with the following amended paragraph:

Figure 15 Scheme 1— *Introduction of a secondary pharmacophore (ketone)*

[0123] Figure 15 Scheme 1 illustrates general methods that can be used for preparation of compounds of the invention having a secondary pharmacophore that is a ketone functional group. While the figure scheme is provided for the synthesis of 1-(3-chlorophenyl)-3-(4-oxodecyl)urea, one of skill in the art will understand that a number of commercially available isocyanates could be used in place of 3-chlorophenyl isocyanate, and that shorter or longer analogs of ethyl 4-aminobutyric acid or hexylbromide could also be employed.

IV. Please replace paragraph [0124] with the following amended paragraph:

[0124] As shown in Figure 15 Scheme 1, ethyl 4-aminobutyrate hydrochloride (available from Aldrich Chemical Co., Milwaukee, Wisconsin, USA) is combined with benzophenone imine at room temperature to provide intermediate (i). DIBAL reduction of the ester group provides an unisolated aldehyde moiety that is then reacted with a suitable Grignard reagent (prepared in situ) to provide intermediate alcohol (ii). Oxidation of the alcohol moiety to a ketone provides (iii) which can then be deprotected to form the amino-ketone (iv). Reaction of (iv) with a suitable isocyanate provides the target compound (794). Substitution of 3-chlorophenyl isocyanate with, for example, adamantyl isocyanate or cyclohexyl isocyanate (also available from Aldrich Chemical Co.) provides other preferred compounds of the invention.

V. Please replace paragraph [0125] with the following amended paragraph:

[0125] As shown in **Figure 16 Scheme 2**, a variety of compounds having a secondary pharmacophore that is either an ester or amide functional group can be prepared. Beginning with 4-aminobutyric acid, treatment with a suitable cycloalkyl or aryl isocyanate provides the urea intermediates shown as (v), wherein R is 3-chlorophenyl, cyclohexyl or 1-adamantyl. Of course other suitable isocyanates can also be employed to provide desired urea intermediates. Esterification via alkylation of the carboxylic acid present in (v) with, for example, pentyl bromide provides the target compounds **767**, **772** and **789**. A variety of suitable alkyl halides can be used to prepare other compounds of the invention. The second path illustrated in **Figure 16 Scheme 2** can be used to prepare compounds such as **768**, as well as those compounds having a primary pharmacophore that is a carbamate. Accordingly, treatment of 4-aminobutyric acid with di-*t*-butyl dicarbonate provides the *t*-butyl carbamate acid (vi) that is converted to a desired amide (vii) using pentylamine, for example, in a mild procedure employing isobutyl chloroformate, and N-methyl morpholine (NMM). Removal of the carbamate protecting group (as it is used in this instance) followed by formation of a urea with a suitable isocyanate (shown here as 3-chlorophenyl isocyanate) provides the target compounds (e.g., **768**).

VI. Please replace paragraph [0126] with the following amended paragraph:

[0126] **Figure 17 Scheme 3** illustrates a variety of methods for introducing secondary pharmacophores that are esters, amide, ureas, carbonates and carbamates, from readily accessible starting materials. In A, ethanolamine is treated with a suitable isocyanate to introduce a primary pharmacophore that is a urea and form intermediate (viii). Treatment of (viii) with an anhydride, a chloro formic acid ester or an isocyanate provides compounds such as **761**, **760** and **762**, respectively. Similar methodology is employed in B, with the addition of protection/deprotection steps. Accordingly, ethylenediamine is monoprotected as a *t*-butyl carbamate. The free amine is then converted to a secondary pharmacophore that is an amide, carbamate or urea using reactants and conditions similar to those employed in "A" to provide intermediates (x). Deprotection of (x) and reaction with a suitable isocyanate provides the target compounds **765**, **777** and **766**. Again, use of isocyanates other than 3-chlorophenyl isocyanate

leads to other compounds of the invention, while substitution of certain reactants used, for example, in the conversion of (ix) to (x) can provide still other compounds of the invention.

VII. Please replace paragraph [0127] with the following amended paragraph:

[0127] **Figure 18 Scheme 4** illustrates pathways for the introduction of a tertiary pharmacophore that is an ester or an amide functional group. In each case, a carboxylic acid group is converted to the desired ester or amide. As shown in **Figure 18 Scheme 4**, 12-aminododecanoic acid (Aldrich Chemical Co.) is converted to urea (687) upon treatment with adamantyl isocyanate. One of skill in the art will appreciate that a variety of alkyl, aryl and cycloalkyl isocyanates can be similarly employed to form other ureas as the primary pharmacophore. Similarly, 11-aminoundecanoic acid or another long chain amino fatty acid could be used in place of 12-aminododecanoic acid. The carboxylic acid moiety can then be esterified or converted to an amide moiety following standard procedures to provide, for example, 780-785, 788 and 800-804 (as esters) and 786, 787, 792 and 793 (as esters and amides).

VIII. Please replace paragraph [0130] with the following amended paragraph:

[0130] Lower case bolded Roman numerals in the examples below refer to the corresponding intermediates in **Figures 15-18 Schemes 1-4 above**. Compounds numbers are also used as provided in the **Figures Schemes** as well as in the Tables below.